UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/608,804	06/30/2003	Nobuko Yamamoto	03500.015716.1	2559

5514 7590 10/16/2009

FITZPATRICK CELLA HARPER & SCINTO
1290 Avenue of the Americas
NEW YORK, NY 10104-3800

EXAMINER	
BAUSCH, SARAE L	
ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
10/16/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/608,804	YAMAMOTO ET AL.	
	Examiner	Art Unit	
	Sarae Bausch PhD	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *74-76 and 79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *74-76 and 79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/03/2009 has been entered.

2. Currently, claims 74-76 and 79 are pending in the instant application. Claims 1-73 and 77-78 are canceled and claim 79 is newly added. All the amendments and arguments have been thoroughly reviewed but were found insufficient to place the instantly examined claims in condition for allowance. The following rejections are either newly presented, as necessitated by amendment, or are reiterated from the previous office action. Any rejection not reiterated below has been withdrawn, necessitated by the amendment to the claims. Response to arguments follow.

New Grounds of Rejection

Claim Rejections - 35 USC § 112- New Matter

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 74-76 and 79 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 74 with the recitation of "square section 500 μm to 6 mm" is not supported in the specification and raises the issue of new matter. The specification does not teach a range for the for the size of square section. The specificaiton teaches a matrices with a region of 1mm by 1mm (see substitute specificaiton page 13, line 6), a density of matrices that is a 500 μm square (see page 15, line 20), thickness of the matrix is 1 to 20 μm (see page 19, line 35), spots that are 500, 100, and 20 μm (see page 33, line 25-29), a 6 mm and 1.2 mm square section (see page 34, lines 11-15), and a glass substrate of 60 mm x 50 mm with a well that is 1 mm x 1mm square. The specification provides no indication of the criticality of the amended range and provides no example of any actual assay which demonstrates variable square sizes or substrate in the amended range. There is no support in the specification to use a square sections of 500 μm to 6 mm that are arranged in a matrix form having no height partitioning the sections. As discussed in MPEP 2163.05, section III, with respect to changing numerical range limitations, the analysis must take into account which ranges one skilled in the art would consider inherently supported by the discussion in the original disclosure. Purdue Pharma L.P. v. Faulding Inc., 230 F.3d 1320, 1328, 56 USPQ2d1481, 1487 (Fed. Cir. 2000) ("[T]he specification does not clearly disclose to the skilled artisan that the inventors... considered the... ratio to be part of their invention.... There is therefore no force to Purdue's argument that the written description requirement was satisfied because the disclosure revealed a broad invention from which the [later-filed] claims carved out a patentable portion").

Claims 74 with the recitation "without a height dividing the plurality of square sections" is not supported in the specification and raises the issue of new matter. The specification teaches a detection substrate with sections separated by wells (walls) of the frame structure matrix patterns (see page 28, line 35-36). The specificaiton discloses the use of a hydrophobic wall on the detection substrate (See page 29, lines 1-5 and page 41, lines 10-15).. The specification further exemplifies the rectangular sections are each spatially isolated by matrix components that with surrounding walls (see page 31, line 13-16). The specificaiton exemplifies sectional view of the support in figure 2B, which depicts a height separating the square sections. The specificiaotn does not disclose the use of a substrate that has square sections that are arranged in a mtric form on a solid substrate that has no height separating the sections. There is no support in the specification to use a substrate with square sections that is not separated by heights. The specification is limited to a substrate that is made of walls and wells.

The response points to separating sections without height may be found in example 1, 5, as well as figures 5, 7, and 8. The response asserts that the figures show an array as discussed in example 1 with adjacent wells separated from each other by black matrix walls and point to figure 7 and 8 as not having walls. As stated in MPEP 2125, When the reference does not disclose that the drawings are to scale and is silent as to dimensions, arguments based on measurement of the drawing features are of little value. See Hockerson-Halberstadt, Inc. v. Avia Group Int 'l, 222 F.3d 951, 956, 55 USPQ2d 1487, 1491 (Fed. Cir. 2000) (The disclosure gave no indication that the drawings were drawn to scale. "[I]t is well established that patent drawings do not define the precise proportions of the elements and may not be relied on to show particular sizes if the specification is completely silent on the issue."). Thus the specification does not

describe that the blank spaces in figures 7 and 8 depict square sections separated by on a solid substrate without heights (walls) as asserted by applicant. Additionally, the specification envisions the use of walls, heights to separate the matrix, see pp. 43-45 and does not contemplate the use of a matrix without a height. Additionally, example 1 clearly exemplifies the use of wells and thus demonstrates that a height separates the sections (See pg. 51, lines 29-34 and pg. 52 lines 5-10). The specification does not define a black matrix as a section on the support without a height and thus the term "black matrix" that separates the sections can not be relied upon for support for without heights between the square sections. The specification describes the black matrix as material that curbs the reflection of the material formed for the matrix, thus the matrix may have a height, and the recitation of black matrix merely requires a black pigment to reflect the resin matrix. Additionally the specification clearly contemplates that the matrix, height from the solid surface is generally 1 to 20 μm (see pg. 19-20). Thus the specification does not provide support for square sections arranged in a matrix form without a height dividing the square sections.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 74-75 are rejected under 35 U.S.C. 102(b) as being anticipated by Brown (US Patent 5807522).

Brown et al. teach a method of detecting differential expression of each of a plurality of genes in a first cell type with respect to expression of the same genes in a second cell type (see column 4, lines 52-59). Brown et al. teach mixtures of labeled cDNA from the two cell types is added to an array of polynucleotides representing a plurality of known genes (see column 4, lines 60-63). Brown et al. teach the array is examined by fluorescence to determine the relative expression of known genes in the two cell types by each spot (see column 4, lines 64-67 and column 5, lines 1-5). Brown et al. spotting polynucleotides of about 50 bp on the array surface and a small volume of labeled DNA probe mixture in a standard hybridization solution is loaded onto each cell and incubation at appropriate temperatures for hybridization by reaction with detection reagents and analyzed using calorimetric, radioactive, or fluorescent detection (see column 13, lines 10-46). Brown et al. teach 100 DNA fragments representing all known mutations of a given gene fabricated on an array (fixing plural types of oligonucleotides having known base sequence different from one another). Brown et al. teach an array of regions on a solid support comprising a two dimensional array with discrete regions having a finite area (see column 6, lines 29-32) and teach the 96 cell array is about 1 to 30 mm in width and 1 to 50 mm in length (see column 11, lines 62-67). Brown et al. teach the array is formed in a plurality of analyte-specific reagent regions, each region may include a different analyte-specific reagent and teach the 96 microarrays assayed with 96 patient samples are incubated, rinsed, detected, and analyzed using standard calorimetric, radioactive, or fluorescent detection and teaches the process can be reversed where the patient or organism's DNA is immobilized as the array elements and each array is hybridized with a different mutated allele or genetic marker (claim 75) (see column 15, lines 18-51).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown (US Patent 5807522) in view of Southern (US Patent 5700637).

Brown et al. teach a method of detecting differential expression of each of a plurality of genes in a first cell type with respect to expression of the same genes in a second cell type (see column 4, lines 52-59). Brown et al. teach mixtures of labeled cDNA from the two cell types is added to an array of polynucleotides representing a plurality of known genes (see column 4, lines 60-63). Brown et al. teach the array is formed in a plurality of analyte-specific reagent regions, each region may include a different analyte-specific reagent and teach the 96 microarrays assayed with 96 patient samples are incubated, rinsed, detected, and analyzed using standard calorimetric, radioactive, or fluorescent detection and teaches the process can be reversed where

the patient or organism's DNA is immobilized as the array elements and each array is hybridized with a different mutated allele or genetic marker (claim 75) (see column 15, lines 18-51). Brown however does not teach application of samples by ink jet method.

However, Southern teaches that ink jet methods of nucleic acids to nucleic acid arrays were well known in the art. Southern teaches that spots can be laid down with a low cost ink jet printer (see column 6 lines 53-56).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to include ink jet method of applying samples to nucleic acid array as taught by Southern in the method of Brown. The ordinary artisan would have been motivated to include an ink jet method for applying a sample to the nucleic acid method and array of Brown because Brown teaches automation of handling fluids to allow for multiple assay to be performed concurrently and Southern teaches that spots can be laid down on a nucleic acid array using a low cost ink jet printer for the expected benefit of a low cost method for multiplexing as taught by Southern and Brown. The ordinary artisan would have had a reasonable expectation of success that the use of ink jet method of Southern could be used for application of a sample to the array of Brown because both Brown and Southern teach nucleic acid array hybridization and spotting of nucleic acids on a solid support for detection of nucleic acids.

10. Claim 79 rejected under 35 U.S.C. 103(a) as being unpatentable over Brown in view of Southern as applied to claim 76 above, and further in view of Drmanac (US Patent 6383742).

The method of Brown in view Southern is set forth above. Brown in view of Southern does not specifically teach that the diameter of each spot is not more than 100 μm.

However, spots of varying size for nucleic acids arrays were well known in the art, including the size of 100 μm. Drmanac et al teach probe spots on nucleic acid array of 100 μm in size (see example 4) (see column 9 lines 1-5).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to include a sample spot size not to exceed 100 μm as taught by Drmanac in the method of Brown in view of Southern in order to produce an array comprising predetermined spot sizes to allow for prevention of contaminating spots of probes and samples on the nucleic acid array as was well known in the art as taught by Drmanac. One of ordinary skill in the art would have been motivated to include sample spots sizes of 100 μm with the substrate of Brown in view of Southern as taught by Dramanac because both Brown in view of Southern and Dramanac teach hybridization of nucleic acid to detect sequences in a nucleic acid sample by nucleic acid hybridization on an array substrate. Furthermore the ordinary artisan would have had a reasonable expectation of success that sample spot diameter of 100 μm and spot density as taught by Drmanac could be used in the method of Brown in view of Southern as both Brown in view of Southern and Dramanac teach nucleic acid hybridization array detection to yield a predictable outcome of detecting nucleic acid target sequences.

11. Claims 74-76 and 79 are rejected under 35 U.S.C. 102(b) as being unpatentable by Southern et al. (US Patent 5700637 published Dec. 23 1997) in view of Dramanc (US Patent 6383742).

Southern et al. teach an apparatus and method for analyzing a polynucleotide sequence of a known or unknown sequence. Southern et al. teach an apparatus comprising a support and attached to the surface a complete set of oligonucleotides of chosen lengths occupying separate

cells and being capable of taking part in hybridization reactions (object component capable of binding to the oligonucleotide) (see column 1, lines 35-47). Southern et al. teach the use of a support by applying labeled material under hybridization conditions to the array to observe the location of the label on the surface associated with particular members of the oligonucleotides (see column 1, lines 52-60). Southern et al. teach preparing a substrate with a plurality of regions (squares) and teaches stripes that 1mm long (side length) (see column 14, lines 48-50). Southern et al. teach the spots can be laid down with a low cost ink jet printer (see column 6, lines 53-56) (claim 76). Southern et al. teach that adding a plurality of oligonucleotides with two different bases in a rectangular patch on the substrate (fixing plural types of oligonucleotides having known base sequences different from one another and present at a uniform surface density in each section) (claim 75) (see column 10, lines 1-6 and example 3). Southern et al. teach preparing clinical samples of three different DNA samples and applying these probes in liquid sample to the surface carrying six oligonucleotide strips and detecting the hybridization signal (detecting whether a complex formed between the oligonucleotide and object component) (see column 12, lines 1-23, example 6). Southern does not teach test samples of 64 to 3600 or sample spot sizes of 100 μm.

However, it was well known in the art that sample sizes of tens, hundreds, and thousands could be analyzed by nucleic acid hybridization array and was well known in the art the spotting of sample size can vary and can include a density of 100 μm, as it taught by Drmanac. Drmanac teaches nucleic acid hybridization by spotting DNA samples on a support such as a nylon membrane and teach that samples in one subarrays can contain 64 sample (see example 8). Thus Drmanac teach analysis of at least 64 test samples in one square section, subarray by

nucleic acid hybridization. Additionally, Drmanac teach the spot size density can be 100 μm (see example 4).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to include a sample sizes of at least 64 samples and include a spot size not to exceed 100 μm as taught by Drmanac in the method of Southern in order to produce an array comprising predetermined spot sizes to allow for prevention of contaminating spots of probes and provide analysis of multiple samples on the nucleic acid array as was well known in the art as taught by Drmanac. One of ordinary skill in the art would have been motivated to include sample spots sizes of 100 μm and include analysis of at least 64 different samples with the substrate of Southern as taught by Dramanac because both Southern and Dramanac teach hybridization of nucleic acid to detect sequences in a nucleic acid sample by nucleic acid hybridization on an array substrate. Furthermore the ordinary artisan would have had a reasonable expectation of success that sample spot diameter of 100 μm and spot density as taught by Drmanac as well as the sample size of 64 samples could be used in the method of Southern as both Southern and Dramanac teach nucleic acid hybridization array detection to yield a predictable outcome of detecting nucleic acid target sequences.

Conclusion

12. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch whose telephone number is (571) 272-2912. The examiner can normally be reached on M-F 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Sarae Bausch/
Primary Examiner, Art Unit 1634